Free radicals are formed by normal physiological processes, from exposures to environmental agents such as pollution, from alcohol consumption, and from cigarette smoke. The damage they do to cells is known as oxidant stress.

For a number of years, work has been done indicating that arachidonic acid—a lipid substrate found in cell membranes throughout the body—may be attacked by free radicals and oxidized and that the resulting products are detectable in the body. "We took that one step further and developed a very specific assay for one of those products so we could look with precision at its formation," said FitzGerald.

The biomarker identified by FitzGerald's team—called 8-epi prostaglandin F2α (8-epi PGF2α)—is one of the isoeicosanoids, a group of 20-carbon molecules that result from free-radical attack on arachidonic acid. It is found in blood and urine. "The attraction of this [marker] is you can actually look in living human beings and get insight into the process," said FitzGerald.

The researchers examined several facets of the free radical question by studying the levels of 8-epi PGF2α in the urine of 24 chronic cigarette smokers.

One endpoint investigated was the relationship between levels of the biomarker and the number of cigarettes smoked, to see that the signal diminished when people quit smoking and switched to nicotine patches. Within that context, said FitzGerald, "We thought we'd get some preliminary information on whether antioxidant vitamins might also depress this marker, which one would suspect they might."

The reason scientists would expect this effect is because the body uses antioxidant compounds found in fruits and vegetables and supplemental vitamins such as C and E to neutralize the effects of free radicals. Excessive free radical generation tends to deplete the body's antioxidant levels, so that smokers tend to have lower vitamin C levels than nonsmokers. The study confirmed FitzGerald's suspicions. According to the paper, "Excretion [of the marker] is dose-dependently increased in apparently healthy chronic cigarette smokers and falls when they switch to nicotine patches." The researchers also found a direct relationship between the number of cigarettes smoked and higher marker levels.

To measure the effects of vitamins C and E on free radical cellular damage, both vitamins were administered individually and in combination to the test subjects. After the chronic smokers took 2 g of vitamin C daily for 5 days, an average 29% decline in the level of 8-epi PGF2α was observed in their urine. Vitamin E by itself was not effective, when 800 IU of vitamin E were given along with 2 g of vitamin C daily for 5 days, an average 23% decline in urinary levels of the marker was found. However, noted FitzGerald, "We've [since] done studies extended in time and over different dose ranges, and have certainly shown that vitamin E will depress this marker as well."

FitzGerald and his colleagues are currently working to determine optimum doses of vitamins to be used as antioxidants, and are studying other drugs thought to be antioxidants as well.

EHPnet

Toward Curing the Tobacco Problem

According to the Centers for Disease Control and Prevention, approximately 418,690 people in the United States die each year due to cigarette smoking. Such disturbing statistics have brought the debate over tobacco use into the political spotlight, but in many instances the energetic appeals and campaigns from both sides of the debate have obscured the facts and confused the public. As an example, though researchers have found that the chances of dying from lung cancer are much greater for smokers, (around 6–13%), a survey published in the 7 June 1993 issue of *The New York Times* showed that both smokers and nonsmokers guessed the chances were closer to 40–50%. One step in addressing this serious public health threat is separating the facts from the hype, and a good place to begin doing this is on the World Wide Web, in particular, the Nicotine and Tobacco Network known as NicNet.

NicNet, a web site maintained by students and faculty at the University of Arizona, contains information about tobacco use and provides links to sites where users can research tobacco-related issues. Though the site, located at <www.ahsc.arizona.edu/nicnet>, takes a clear stance against the use of tobacco, it also provides links to both tobacco industry and personal pro-tobacco sites (accessible by following the Pro-Tobacco Point of View link). To include NicNet users in the tobacco debate, the site's administrators maintain a listserv discussion group which can be joined by following the Tobactalk link on the homepage.

For more fact-based information, users can access the Tobacco Library link. Resources available here include links to the web sites of relevant journals (via the Tobacco Literature link) and a News You Can Use link that allows users to search newspapers for tobacco-related articles, and the Health Issues link allows users to access various sites and articles on cancer, epidemiology, and the actions of the federal health agencies. Under the Grants & Funding link, scientists can obtain information on where to find the capital to conduct tobacco-related research. The Policy & Legal Issues link provides access to documents ranging from a 1988 Surgeon General's report to an archive (located at the University of California–San Francisco) from the Brown & Williamson Tobacco Company. Via the Research link users can access to and search the U.S. legislative record and other federal documents.

Information on the Society for Research on Nicotine and Tobacco is included at the NicNet site and include how to join the society, information about available grants for cancer and tobacco studies, including $6 million made available by the Robert Wood Johnson foundation, and guidelines for administering drugs with abuse potential to humans involved in research studies.

NicNet also provides comprehensive resources to help smokers quit and to help parents keep their children away from tobacco. Additionally, there is a Nicotine/Tobacco Link of the Week and a Health Site of the Day featured on the homepage, providing users with an ever-changing list of resources to help educate them on the tobacco debate.